



1645

Docket No. 55293-B-PCT-US/JPW/AJM/MVM

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Carlos Cordon-Cardo et al.
Serial No.: 10/009,861 Examiner: Not Yet Known
Filed : December 10, 2001 Group Art Unit: 1645
For : MARKERS FOR PROSTATE CANCER

1185 Avenue of the Americas
New York, New York 10036
February 28, 2003

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

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SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

TECH CENTER 1600/2900

In accordance with the duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following references which are listed on Form PTO-1449 (**Exhibit A**).

1. PCT International Application No. PCT/US98/14566, filed July 14, 1998, International Publication No. WO99/04238, published January 28, 1999;
2. PCT International Application No. PCT/US98/01922, filed January 29, 1998, International Publication No. WO98/33450, published August 6, 1998;
3. PCT International Application No. PCT/US94/03528, filed March 30, 1994, International Publication No. WO94/22478 A, published October 13, 1994;
4. PCT International Application No. PCT/US98/26266, filed

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Page 2

December 10, 1998, International Publication No. WO99/31140 A,
published June 24, 1999;

5. Aaltomaa, S. et al. (1999) "Prognostic Value and Expression of p21 (waf1/cip1) Protein in Prostate Cancer" *The Prostate*, 39(1):8-15;
6. Agus, D.B. et al. (1999) "Response of Prostate Cancer to Anti-HER-2/neu Antibody in Androgen Dependent and -Independent Human Xenograft Models" *Cancer Research*, 59(1):4761-4764;
7. Arai, Y. et al. (1997) "C-erbB-2 Oncoprotein: A Potential Biomarker of Advanced Prostate Cancer" *Prostate*, 30(3):195-201;
8. Baretton, G.B. et al. (1999) "Proliferation- and Apoptosis-Associated Factors in Advanced Prostatic Carcinomas Before and After Androgen Deprivation Therapy: Prognostic Significance of p21/WAF1/CIP1 Expression" *British Journal of Cancer*, 80(3-4):546-555;
9. Baselga, J. et al., (1998) "Recombinant Humanized Anti-HER2 Antibody (Herceptin TM) Enhances the Antitumor Activity of Paclitaxel and Doxorubicin Against HER2/neu Overexpressing Human Breast Cancer Xenografts" 58(13):2825-2831;
10. Cariou S. et al. (1998) "Prognostic Implication of Expression of the Cell Cycle Inhibitor Protein P27", *Breast Cancer Research and Treatment*, 1-3(52):29-41;

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11. Cordon-Cardo Carlos, et al. (1998) "Distinct Altered Patterns of p27^{KIP1} Gene Expression in Benign Prostatic Hyperplasia and Prostatic Carcinoma" *J. Natl. Cancer Inst.* 90(17): 1284-1291;
12. Cote, R.J. et al. (1998) "Association of p27^{KIP1} Levels With Recurrence and Survival in Patients With Stage C Prostate Carcinoma" *J. Natl. Cancer Inst.* 90(12): 916-920;
13. Chen, Y. et al. (1998) "Increased Cell Growth and Tumorigenicity in Human Prostate LNCaP Cells by Overexpression to Cyclin D1" *Oncogene*, 16(15):1913-1920;
14. Craft, N. et al., (1999) "A Mechanism for Hormone-Independent Prostate Cancer Through Modulation of Androgen Receptor Signaling by the HER-2/neu tyrosine Kinase" *Nature Medicine*, 5(3):280-285;
15. Curnow, R.T. et al., (1997) "Clinical Experience With CD64-Directed Immunotherapy. An Overview" *Cancer Immunology And Immunotherapy*, 45(3-4):210-15;
16. Database Biosis [Online] Biosciences Information Service, Philadelphia, PA, US (1999-03) Lee Tae Yoon et al., "Immunohistochemical Expression of p53 and MDM-2 Protein in Various Epithelial Carcinomas" Database Accession No. PREV1999900406745;
17. DeMarzo, A.M. et al. (1998) "Prostate Stem Cell Compartments:

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Page 4

Expression of the Cell Cycle Inhibitor p27kip1 in Normal, Hyperplastic, and Neoplastic Cells" *Amer. J. Path.* 153(3): 911-919;

18. Fernandez, P.L. et al. (1999) "Expression of p27/kip1 Is Down-regulated in Human Prostate Carcinoma Progression" *J. Path.* 187 (5): 563-566;
19. Gumbiner, L. et al. (1999) "Overexpression of Cyclin D1 Is Rare in Human Prostate Carcinoma" *Prostate*, 38(1):40-45;
20. Guo, Y. et al. (1997) "Loss of the Cyclin-dependent Kinase Inhibitor p27^{Kip1} Protein in Human Prostate Cancer Correlates with Tumor Grade¹" *Clin. Cancer Res.* 3:2269-2274;
21. Han, E. et al., (1998) "Cyclin D1 Expression in Human Prostate Carcinoma Cell Lines and Primary Tumors" *Prostate*, 35(2):95-101;
22. James, N. et al., (1998) "Phase II Trial of the Bispecific Antibody MDX-H210 (Anti-Her2/Neu X Anti-CD64) Combined With GM-CSF In Patients With Advanced Prostate and Renal Cell Carcinomas That Express Her2/Neu" *British Journal of Cancer*, 78(Suppl 2):19;
23. Koeneman, K.S. et al., (1999) "Osteomimetic Properties of Prostate Cancer Cells: A Hypothesis Supporting the Predilection of Prostate Cancer Metastasis and Growth in the Bone Environment" *Prostate*, 39:246-261;

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Page 5

24. Lee, C.T. et al., (1999) "Overexpression of the Cyclin-Dependent Kinase Inhibitor P16 is Associated with Tumor Recurrence in Human Prostate Cancer" *Clinical Cancer Research, The American Association for Cancer Research, US*, 5(5):977-983;
25. Lloyd et al. (1999) "P27^{kip1}: a Multifunctional Cyclin-dependent Kinase Inhibitor with Prognostic Significance in Human Cancers" *American J. Pathology* 154(2): 313-323;
26. McArthur, J.G. et al. (1999) "Cancer Gene Therapy with Novel Chimeric P27/p16 Tumor Suppressor Genes" *Proceed. Amer. Assoc. Cancer Res. Ann.* 40: 630;
27. Osman, I. et al. (1999) "Inactivation of the p53 Pathway in Prostate Cancer: Impact on Tumor Progression" *Clinical Cancer Research: An Official Journal of the American Association for Cancer Research*, 5(8):2082-2088;
28. Ross, J.S. et al., (1993) "Contribution of HER-2/neu Oncogene Expression to Tumor Grade and DNA Content Analysis in the Prediction of Prostatic Carcinoma Metastasis" *Cancer*, 72(10):3020-3028;
29. Veltri, R. et al. (1994) "Quantitative nuclear morphometry, Markovian Texture Descriptors, and DNA content Captured on a CAS-200 Image Analysis Systems, Combined With PCNA and HER-2/neu Immunohistochemistry for Prediction of Prostate Cancer

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Page 6

Progression" *Journal of Cellular Biochemistry*, 19:249-258;

30. Yamasaki, I. et al. (1996) "Overexpression of MDM2 and p53 Protein is Infrequently but Significantly Associated With Progression of Human Prostatic Adenocarcinoma" *Oncology Reports*, 3(5):925-929; and
31. Zhau, H. et al. (1992) "Expression of C-erb B-2/neu Proto-Oncogene in Human Prostatic Cancer Tissues and Cell Lines" *Molecular Carcinogenesis*, 5(4): 320-327.

The subject application is a §371 national stage application and claims the benefit under 35 U.S.C. §120 of PCT International Application No. PCT/US00/16007, filed June 9, 2000, which is a continuation-in-part and claims benefit under 35 U.S.C. §120 of U.S. Serial No. 09/329,917, filed June 10, 1999.

The above-listed references 2, 5-11, 13, 15-20 and 23-30 were submitted to and considered by the United States Patent and Trademark Office in an Information Disclosure Statement filed on May 23, 2000 in connection with U.S. Serial No. 09/329,917, filed June 10, 1999. Also, above-listed reference 1 was cited by the United States Patent and Trademark Office in a Final Office Action dated December 20, 2001 in connection with U.S. Serial No. 09/329,917, filed June 10, 1999. Accordingly, under 37 C.F.R. §1.98(d) copies of these references are not required to be provided to the United States Patent and Trademark Office, since they were previously submitted to or cited by the United States Patent and

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Trademark Office in an application relied upon for an earlier filing date under 35 U.S.C. §120.

A Supplementary Partial European Search Report was issued on November 29, 2002 in connection with European Application No. EP 00938256.5, which is a related foreign counterpart of the subject application. A copy of the Supplementary Partial European Search Report is attached hereto as **Exhibit B**. Above-listed references 1-31 were cited in the Supplementary Partial European Search Report. References 6, 11-12, 20, 24 and 27 were submitted to and considered by the United States Patent and Trademark Office in an Information Disclosure Statement filed on May 23, 2000 in connection with U.S. Serial No. 09/329,917, filed June 10, 1999. Reference 25 was submitted to and considered by the United States Patent and Trademark Office in a Supplemental Information Disclosure Statement filed on December 19, 2000 in connection with U.S. Serial No. 09/329,917, filed June 10, 1999. References 1-2, 17-18 and 26 were submitted to and considered by the United States Patent and Trademark Office in a Supplemental Information Disclosure Statement filed on October 10, 2002 in connection with U.S. Serial No. 09/329,917, filed June 10, 1999. References 3-5, 7-10, 13-16, 19, 21-23 and 28-31 are being submitted concurrently to the United States Patent and Trademark Office in a Supplemental Information Disclosure Statement filed on February 28, 2003 in connection with U.S. Serial No. 09/329,917, filed June 10, 1999. Accordingly, under 37 C.F.R. §1.97(d), copies of these references are not required to be provided to the United States Patent and Trademark Office, since they were, or are being concurrently submitted herewith, whichever is applicable, to the United States Patent and Trademark Office in an application relied upon for an earlier filing date under 35

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U.S.C. §120.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

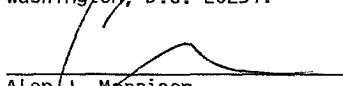
No fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



John P. White
Registration No. 28,678
Alan J. Morrison
Registration No. 37,399
Attorneys for Applicant(s)
Cooper & Dunham, LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.


Alan J. Morrison
Reg. No. 37,399

2/28/03
Date

Form PTO-1449

U.S. Department of Commerce
Patent and Trademark OfficeAtty. Docket No.
1747/55293-B-PCT-
US/JPW/AJM/MVMSerial No.
10/009,861

INFORMATION DISCLOSURE STATEMENT

(Use several sheets if necessary)

Applicant
Carlos Cordon-Cardo et al.Filing Date
December 10, 2001Group
1634

U.S. PATENT DOCUMENTS

Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate

FOREIGN PATENT DOCUMENTS

	Document Number	Date	Country	Class	Subclass	Translation	
						Yes	No
	WO 9 9 0 4 2 3 8	1/28/99	PCT				
	WO 9 8 3 3 4 5 0	5/6/98	PCT				
	WO 9 4 2 2 4 7 8	10/13/94	PCT				
	WO 9 9 3 1 1 4 0	6/24/99	PCT				

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Aaltomaa, S. et al. (1999) "Prognostic Value and Expression of p21 (waf1/cip1) Protein in Prostate Cancer" <i>The Prostate</i> , 39(1):8-15;
	Agus, D.B. et al. (1999) "Response of Prostate Cancer to Anti-HER-2/neu Antibody in Androgen Dependent and -Independent Human Xenograft Models" <i>Cancer Research</i> , 59(1):4761-4764;
	Arai, Y. et al. (1997) "C-erbB-2 Oncoprotein: A Potential Biomarker of Advanced Prostate Cancer" <i>Prostate</i> , 30(3):195-201;
	Baretton, G.B. et al. (1999) "Proliferation- and Apoptosis-Associated Factors in Advanced Prostatic Carcinomas Before and After Androgen Deprivation Therapy: Prognostic Significance of p21/WAF1/CIP1 Expression" <i>British Journal of Cancer</i> , 80(3-4):546-555;
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EXAMINER

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609: Draw line through citation if not in conformance and not considered. Include copy of this from with next communication to applicant.

Applicants: Carlos Cordon-Cardo et al.
Serial No.: 10/009,861
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Exhibit A

Form PTO-1449

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					Yes	No

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

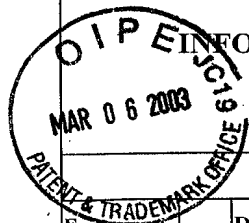
	Cariou S. et al. (1998) "Prognostic Implication of Expression of the Cell Cycle Inhibitor Protein P27", <i>Breast Cancer Research and Treatment</i> , 1-3(52):29-41;
	Cordon-Cardo Carlos, et al. (1998) "Distinct Altered Patterns of p27 ^{KIP1} Gene Expression in Benign Prostatic Hyperplasia and Prostatic Carcinoma" <i>J. Natl. Cancer Inst.</i> 90(17): 1284-1291;
	Cote, R.J. et al. (1998) "Association of p27 ^{KIP1} Levels With Recurrence and Survival in Patients With Stage C Prostate Carcinoma" <i>J. Natl. Cancer Inst.</i> 90(12): 916-920;
	Chen, Y. et al. (1998) "Increased Cell Growth and Tumorigenicity in Human Prostate LNCaP Cells by Overexpression to Cyclin D1" <i>Oncogene</i> , 16(15):1913-1920;

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	Craft, N. et al., (1999) "A Mechanism for Hormone-Independent Prostate Cancer Through Modulation of Androgen Receptor Signaling by the HER-2/neu tyrosine Kinase" <i>Nature Medicine</i> , 5(3):280-285;
	Curnow, R.T. et al., (1997) "Clinical Experience With CD64-Directed Immunotherapy. An Overview" <i>Cancer Immunology And Immunotherapy</i> , 45(3-4):210-15;
	Database Biosis [Online] Biosciences Information Service, Philadelphia, PA, US (1999-03) Lee Tae Yoon et al., "Immunohistochemical Expression of p53 and MDM-2 Protein in Various Epithelial Carcinomas" Database Accession No. PREV1999900406745;
	DeMarzo, A.M. et al. (1998) "Prostate Stem Cell Compartments: Expression of the Cell Cycle Inhibitor p27kip1 in Normal, Hyperplastic, and Neoplastic Cells" <i>Amer. J. Path.</i> 153(3): 911-919;

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	Fernandez, P.L. et al. (1999) "Expression of p27/kip1 Is Down-regulated in Human Prostate Carcinoma Progression" <i>J. Path.</i> 187 (5): 563-566;
	Gumbiner, L. et al. (1999) "Overexpression of Cyclin D1 Is Rare in Human Prostate Carcinoma" <i>Prostate</i> , 38(1):40-45;
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	Han, E. et al., (1998) "Cyclin D1 Expression in Human Prostate Carcinoma Cell Lines and Primary Tumors" <i>Prostate</i> , 35(2):95-101;

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<div>OFFICE OF PATENT & TRADEMARK MAR 06 2003</div> INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)				Applicant Carlos Cordon-Cardo et al.					
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2280 HV Rijswijk (ZH)
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FAX +31 70 340 3016

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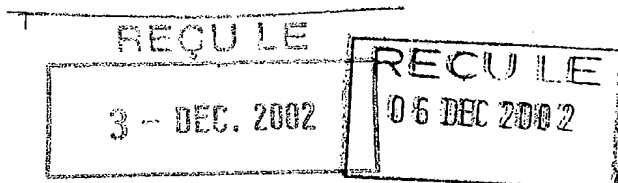
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Patent Office

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Département à
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Ernest Gutmann - Yves Plasseraud S.A.
3, rue Chauveau-Lagarde
75008 Paris
FRANCE



E. GUTMANN - Y. PLASSERAUD S.A.

Datum/Date

29. 11. 02

Zeichen/Ref./Réf. B5149 - CA	Anmeldung Nr./Application No./Demande n°./Patent Nr./Patent No./Brevet n°. 00938256.5
Anmelder/Applicant/Demandeur/Patentinhaber/Proprietor/Titulaire Sloan-Kettering Institute For Cancer Research	

COMMUNICATION

The European Patent Office herewith transmits

- ☐ the European search report
- ☐ the declaration under Rule 45 EPC
- ☐ the partial European search report under Rule 45 EPC
- ☒ the supplementary European search report concerning the international application under Article 157(2) EPC relating to the above-mentioned European patent application. Copies of the documents cited in the search report are enclosed.

The following specifications given by the applicant have been approved by the Search Division :

- ☐ Abstract ☐ Title ☐ Figure
- ☐ The abstract was modified by the Search Division and the definitive text is attached to this communication.
- ☐ The following figure will be published with the abstract, since the Search Division considers that it better characterises the invention than the one indicated by the applicant.
- Figure:
- ☐ Additional copy(copies) of the documents cited in the European search report.

REFUND OF THE SEARCH FEE

If applicable under Article 10 Rules relating to fees, a separate communication from the Receiving Section on the refund of the search fee will be sent later.



EPO Form 1507 02.93

Applicants: Carlos Cordon-Cardo et al.
Serial No.: 10/009,861
Filing Date: December 10, 2001
Exhibit B



European Patent
Office

Application Number
EP 00 93 8256

CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing more than ten claims.

- ☐ Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid, namely claim(s):
- ☐ No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

- ☒ All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.
- ☐ As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.
- ☐ Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:
- ☐ None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:



European Patent
Office

**LACK OF UNITY OF INVENTION
SHEET B**

Application Number
EP 00 93 8256

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims: 1-4, 6-9, 11-12, 26-27

Methods, uses, and compositions relating to p27.

2. Claims: 14, 28

Methods and use relating to p21.

3. Claims: 15, 29

Methods and use relating to mdm2.

4. Claims: 16-17, 30

Methods and use relating to cyclin D1.

5. Claims: 18, 31

Methods and use relating to p16.

6. Claims: 19-25

Uses and methods relating to Her-2/neu.



European Patent
Office

**SUPPLEMENTARY
PARTIAL EUROPEAN SEARCH REPORT**

which under Rule 45 of the European Patent Convention EP 00 93 8256 shall be considered, for the purposes of subsequent proceedings, as the European search report

Application Number

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
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Y	* the whole document *	2,3,6-9, 11,12	
X	WO 98 33450 A (PORTER PEGGY L ;ROBERTS JAMES M (US)) 6 August 1998 (1998-08-06)	1,4,26, 27	
Y	* abstract * * page 4, line 20 - page 5, line 6 * * claims 1-9 * --- -/--	2,3,6-9, 11,12	
			TECHNICAL FIELDS SEARCHED (Int.Cl.7)
			C12Q G01N C07K
The supplementary search report has been based on the last set of claims valid and available at the start of the search.			
INCOMPLETE SEARCH			
The Search Division considers that the present application, or some or all of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for the following claims:			
Claims searched completely :			
Claims searched incompletely :			
Claims not searched :			
Reason for the limitation of the search: see sheet C			
Place of search MUNICH		Date of completion of the search 7 October 2002	Examiner Madlener, M
CATEGORY OF CITED DOCUMENTS		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document			

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EPO FORM 1503 03.82 (P04C20)



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Y	* the whole document *	6-9,11, 12	
X	COTE RICHARD J ET AL: "Association of p27Kip1 levels with recurrence and survival in patients with stage C prostate carcinoma." JOURNAL OF THE NATIONAL CANCER INSTITUTE (BETHESDA), vol. 90, no. 12, 17 June 1998 (1998-06-17), pages 916-920, XP002931303 ISSN: 0027-8874	1,4,26	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
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Y	* abstract * * page 2273, last paragraph * --- -/--	4,6-9,11,12	



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P,X	WO 99 31140 A (GENENTECH INC) 24 June 1999 (1999-06-24) * abstract * * page 3, line 29 - page 4, line 37 * * page 27, line 12 - page 30, line 31 * * claims 1-19 *	19-25	



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X	ARAI YOICHI ET AL: "C-erbB-2 Oncoprotein: A potential biomarker of advanced prostate cancer." PROSTATE, vol. 30, no. 3, 1997, pages 195-201, XP002214672 ISSN: 0270-4137 * abstract *	24,25	

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P,X	AGUS D B ET AL: "RESPONSE OF PROSTATE CANCER TO ANTI-HER-2/NEU ANTIBODY IN ANDROGEN DEPENDENT AND -INDEPENDENT HUMAN XENOGRAFT MODELS" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 59, 1 October 1999 (1999-10-01), pages 4761-4764, XP000919490 ISSN: 0008-5472 * abstract * * page 4762 - page 4764 * -----	19-25	TECHNICAL FIELDS SEARCHED (Int.Cl.7)



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INCOMPLETE SEARCH
SHEET C

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Claim(s) searched completely:
1-4, 6-9, 11-12, 14-31

Claim(s) not searched:
5, 10, 13

Reason for the limitation of the search:

Present claims 5, 10 and 13 relate to substances defined by reference to desirable characteristics or properties, namely their capability of inducing p27 protein expression (claim 5) or their capability of stabilizing the p27 protein (claims 10 and 13).

Claims 5, 10 and 13 relate to all substances having one of these characteristics or properties, without relating to any further technical features. However, the application does not provide any according support within the meaning of Article 84 EPC and/or disclosure within the meaning of Article 83 EPC.

Moreover, and independent of the above reasoning, the claims also lack clarity (Article 84 EPC) for the reason that an attempt is made to define the substances only by reference to a result to be achieved (induction of p27 expression; stabilization of the p27 protein). The lack of any other technical feature does not allow the skilled person to clearly and unambiguously understand the scope of the claims. Again, this lack of clarity in the present case is such as to render a meaningful search impossible.

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

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This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

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